

Remarks

The March 19, 2004 Official Action has been carefully considered. In view of the amendments submitted herewith and these remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, it is noted that a shortened statutory response period of three (3) months was set in the March 19, 2004 Official Action. Accordingly, the initial response period is due to expire June 21, 2004, as June 19th falls on a Saturday. This amendment and request for reconsideration is being filed before the expiration of the initial response period.

It is also noted, preliminarily, that claims 2-8, 10, 12, 14, 16-18 and 24-32 have been withdrawn from consideration as a result of applicants' election in response to the restriction requirement dated October 3, 2003. Applicants wish to make clear that the election of claims 1, 9, 11, 13, 15 and 19-23 in response to the aforementioned restriction requirement is without prejudice to applicants' right to file one or more divisional applications, as provided in 35 U.S.C. §121, directed to the subject matter of the withdrawn claims.

In the March 19, 2004 Official Action, the specification is objected to because the title is considered non-descriptive. A new title is included with the present amendment, which is the title suggested by the examiner.

Additional formal objections have been raised with respect to an internet address set forth at page 13 of the

specification and the spelling of the name "Ohnishi" which appears at the top of page 32 of the specification. These informalities have been appropriately addressed in the present amendment.

Turning to the substantive aspects of the March 19, 2004 Official Action, all of the claims presently under consideration stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite in a number of respects. Specifically, the examiner contends that the nature and/or structure of the *scbA* gene for deletion are unclear in the case of *S. lividans*, e.g. in claims 1 and 9. The examiner further asserts that the term "homologue" is unclear as to its exact nature, e.g. in claim 15. Subparagraphs (a) and (b) of claims 19 are characterized as confusing, because the recited portion of EMBL AJ007731 is identical to the recited portion of SEQ ID NO: 19. Also in this connection, the inclusion of an accession number in subparagraph (c) of claim 19 is criticized as lacking clarity and the recitation, "to amplify total DNA of said species or strain", in subparagraph (d) of claim 19, is considered "wholly unclear". The term "about" in claims 19-20 is also considered unclear, as is the recitation of "the level of sequence identity" in claims 20-23.

All of the claims under consideration have been rejected as allegedly failing to comply with the enablement requirement of 35 U.S.C. §112, first paragraph. According to the examiner, the present specification does not reasonably provide enablement

for function deletion of the *scbA* gene, and undue experimentation allegedly would be required to make all the strains having functional deletions of the *scbA* gene encompassed by the claims.

Claims 15 and 19-23 are further rejected under the enablement provision of 35 U.S.C. §112, the examiner asserting in this regard that the specification does not reasonably provide enablement for deleting *scbA* gene homologs in *Streptomyces* without a known homolog.

Claims 15 and 19-23 have also been rejected under 35 U.S.C. §102(b), as allegedly anticipated by Horinouchi et al. (J. Bacteriol 171: 1206-10 (1989)), which is reference C10 in the IDS filed January 28, 2004, and under 35 U.S.C. §102 (a), as allegedly anticipated by Kawachi et al. (Molecular Biology, 36 (2): 302-13 (2000)).

The foregoing objections and rejections constitute all of the grounds set forth in the March 19, 2004 Official Action for refusing the present application.

Lastly, the Examiner has also made of record certain additional references which are referred to by the Examiner as "other notable art". Specifically, Takano, et al (Molecular Microbiology, 41 (5): 1015-28 (2001); Butler et al. (Appl. Microbiol. Biotechnol., 61: 512-16 (2003) and GenBank Accession No. NP 823445 have been made of record , but no rejection has been based on the last mentioned three (3) references. It is noted in this connection that the Examiner acknowledges that none of these references qualifies as prior art.

In accordance with the present amendment, claim 15 has been amended to include a disclaimer of the species *S. virginiae*. Express support for disclaiming *S. virginiae* is provided in the present specification at page 11, lines 24-26. Claim 15 has further been amended to require that the effect of said deletion on increasing said antibiotic production in said anti-biotic producing strain is unknown. Support for this recitation is implicitly provided by the passages in the specification that refer to determining whether or not antibiotic production in a given antibiotic-producing strain of a *Streptomyces* species is increased. If the effect of the gene deletion were known in advance, it would not be necessary to make such a determination.

Claim 19 has been amended by deleting the recitation that the nucleic acid sequence referred to therein is the complement of nucleotides to 2914 to 1970 of EMBL AJ007731. Consequently, the nucleotide sequence of claim 19 is defined in terms of the three (3) remaining characteristics, (a)-(c). The last line of claim 19 has also been amended to read "which produce said amplification product from total DNA of said species or strain. Support for this amendment is provided in the present specification in the paragraph bridging pages 11-12.

Claim 20 has been amended to make more explicit that which is immediately apparent from its original wording, i.e. that the nucleotide sequence of claim 19 encodes a polypeptide having 50% sequence identity with the amino acid sequence of Fig. 10.

Also the words "about" and "the level of" have been omitted from claims 19-23.

No new matter has been introduced into this application by reason of any of the amendments presented herewith. Moreover, none of the present claims amendments is believed to constitute a surrender of any originally claimed subject matter, or a narrowing of the claims in order to establish patentability. The effect of these amendments is to make explicit that which was implicit in the claims as originally worded.

As a result of the present amendment, the 35 U.S.C. §112, second paragraph rejections set out at page 5 of the March 19, 2004 Official Action (§§ 10-12) are believed to be overcome. Thus, the only rejections remaining to be addressed are the 35 U.S.C. § 112, second paragraph, rejections of claims 1, 9, 11, 13, 15 and 19-23 with regard to the allegedly unclear nature and/or structure of the *scbA* gene for deletion in *S. lividans*, and of claims 15 and 19-23 based on the term "homologue"; the above noted rejections based on alleged failure to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph; and the anticipation rejections of claims 15 and 19-23 based on Horinouchi et al. and Kawachi et al, respectively. All of these last-mentioned grounds of rejection are respectfully traversed for the reasons presented hereinbelow.

A. Claim 1, 9, 11, 13, 15 and 19-23 satisfy the definiteness requirement of 35 USC §112 2nd paragraph.

A1. The relevant inquiry in determining compliance with the definiteness requirement of 35 U.S.C. §112, second paragraph, is whether the claim in question sets out and circumscribes a particular area with a sufficient degree of precision and particularity, such that the metes and bounds of the claimed invention are reasonably clear. In re Moore, 169 U.S.P. Q. 236 (C.C.P.A. 1971).

The definiteness of claim language may not be analyzed in the abstract, but must be considered in light of the supporting specification, with the language in question being accorded the broadest reasonable interpretation consistent with its ordinary usage in the art. In re Morris, 44 U.S. P.Q. 2d 1023, 1027 (Fed. Cir. 1997). See also Ex parte Cole, 223 U.S.P.Q. 94 (Bd. App. 1983) (claims are addressed to the person of average skill in a particular art; compliance with §112 must be adjudged from that perspective, not in a vacuum).

Furthermore, it has long been held that the initial burden of establishing a failure to comply with 35 U.S.C. §112, second paragraph, rests upon the Examiner. In rejecting a claim for alleged indefiniteness, therefore, it is incumbent upon the Examiner to establish that one having ordinary skill in the art would not have been able to ascertain the scope of protection defined by the claim when read in light of the supporting specification. Ex parte Cordova, 10 U.S. P.Q.2d 1949, 1952 (PTO

B.P.A.I, 1988).

When the appropriate procedural approach is followed in assessing the claim terminology at issue, in accordance with the above-noted authorities, it is beyond question that applicants have satisfied the definiteness requirement of §112, second paragraph, with respect to the subject matter of claims 1, 9, 11, 13, 15 and 19-23.

Given the nature of the present invention, claims 1, 9, 11, 13, 15 and 19-23 cannot properly be rejected because of the lack of characterization of the *S. lividans scbA* gene. Characterization of the *scbA* gene is not necessary, as applicants' claims require only that the gene be functionally deleted. One's ability to functionally delete the *scbA* gene has nothing to do with the gene's characterization. Indeed, the present specification discloses the methodology for effecting just such a deletion by using a plasmid carrying a deletion mutant of the *S. coelicolor scbA* gene. See example 8.

Turning to the rejection directed at the term "homologue", the Examiner's criticism in this regard is based on a misinterpretation of the relevant disclosure in the specification. Notwithstanding, the Examiner's assertion to the contrary, the specification does not state that a homologue is the gene with the highest sequence identity to *scbA*. Rather, the specification states that a homologue is the gene with the highest sequence identity to *scbA* of all genes of a given strain. A further characterization of the term "homologue" is provided

at page 11 lines 32 through page 12 line 11 of the present specification. Thus, the term "homologue" cannot reasonably be regarded as vague, indefiniteness, or otherwise unclear, when it is properly considered in light of the definition contained in applicants' specification. Cf. In re Morris, supra.

In summary, applicants' position with respect to the rejections of claims 1, 9, 11, 13, 15 and 19-23 based on 35 U.S.C. § 112, second paragraph, is that any person of ordinary skill in the art, having applicants' disclosure and claims before him or her, would be apprised to a reasonable degree of certainty as to the exact subject matter encompassed within the claims 1, 9, 11, 13, 15, 19- 23. Nothing more is required under 35 U.S.C. §112, second paragraph.

For all of the foregoing reasons, it is clear that in the present case, the Examiner has failed to satisfy the PTO's burden of proof with respect to the §112 , second paragraph, rejection of claims 1, 9, 11, 13, 15, 19-23 as set forth in the March 19, 2004 Official Action. Accordingly, this ground of rejection is improper and should be withdrawn.

B. Claims 1, 9, 11, 13, 15, 19-23 fully comply with the enablement requirement of 35 USC §112 first paragraph.

1. The enablement provided in the present specification is commensurate with the full scope of claims 1, 9, 11, 13 15 and 19-23 insofar as concerns the functional deletion of the scbA gene.

The Examiner contends that the scope of enablement provided in the present specification is deficient because all possible means for effecting functional deletion of the *scbA* gene are not exemplified. In order to practice the present invention, however, only one functional deletion is needed - there is no need to be able to predict every possible functional deletion for a given gene, as the Examiner appears to imply. The present specification provides a sequence of the whole *scbA/R/B* gene cluster, including promoter regions. This information allows those skilled in the art to predict multiple functional deletions of the genes in the cluster. Thus, the enablement provided in the present specification is clearly commensurate with the scope of the subject matter claimed in claims 1, 9, 11, 13 15 and 19-23.

2. The enablement provided in the present specification is commensurate with the scope of claims 15 and 19-23 insofar as concerns deleting *scbA* gene homologs in *Streptomyces* without a known homolog.

Applicants respectfully take exception to the Examiner's assertion that claims 15 and 19-23 are not fully enabled because the specification does not permit those of ordinary skill in the art to make functional deletions of *scbA* homologs in other *Streptomyces* species where the homolog is not already known, without undue experimentation.

For those skilled in the art, the identification of homologs in other species is a matter of routine procedure. Knowledge of

the sequence of a *scbA* gene from one species permits those skilled in the art to identify homologs in another species by a variety of routine and standard procedures well known in the art, such as PCR or Northern hybridization. This does not constitute an undue burden, and is certainly not "wholly unpredictable" as the Examiner contends.

Moreover, in certain cases it is not necessary that the homolog be known as a plasmid carrying a *S. coelicolor* deletion mutant can eliminate *scbA* activity in other species, as shown in Example 8 of the present specification.

It is simply not the case that, as the Examiner states, "one of skill in the art must delete genes virtually at random to affect antibiotic production". One of skill in the art would identify a *scbA* homolog and functionally delete it in order to carry out the claimed method. No "random" deletion of genes would be required. It is irrelevant that certain *scbA* homologs in other species do not have the same effect on antibiotic production as *scbA* in *S. coelicolor*, as establishing the effect on antibiotic production is the object of the method of claims 15 and 19-23.

For the reasons stated above, it is respectfully submitted that the guidance provided in the present specification is more than sufficient to satisfy the enablement requirement of 35 USC §112, first paragraph, for the full scope of claims 1, 9, 11, 13, 15 and 19-23. Accordingly, the 35 U.S.C. §112, first paragraph, rejections set forth in paragraph 13 and 14 of the March 19,

2004 official action are untenable and should be withdrawn.

C. The prior art cited in support of the 35 USC §102 rejections of claims 15 and 19-23 fails to constitute evidence of lack of novelty.

Rejections under 35 USC §102 are proper only when the claimed subject matter is identically disclosed or described in the reference cited as evidence of lack of novelty. In re Arkley, 172 USPQ 524 (C.C.P.A. 1972). Applying this rule of law to the present case, the 35 USC §102 rejections of claims 15 and 19-23 based on Horinouchi, et al. and Kawachi, et al, respectively, are improper because the subject matter of those claims is nowhere identically disclosed or described in the cited references.

The method of claim 15 is patentably distinguishable from Horinouchi, et al, because the later does not provide response for the recitation in claim 15 calling for the effect of said deletion on increasing said antibiotic production in said antibiotic-producing strains being unknown. As explained at page 32, lines 3-20 of the present specification, the regulation of antibiotic production in *S. griseus* by *asfA* is fundamentally different from that in *S. coelicolor*, in that the *asfA* mutant, which is equivalent to the *scbA* of the present invention, produces neither streptomycin or A-factor. The *asfA* mutant is thus the reverse phenotype in comparison to the *S. coelicolor* mutant employed in the present invention. As such, claim 15 does not read on the method as applied to *S. griseus*, because the

outcome is already known.

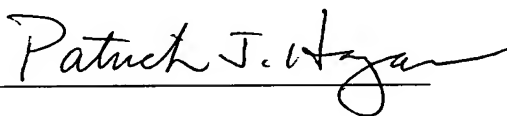
As for the §102(a) rejection of claims 15 and 19-23 based on Kawachi, et al, this rejection cannot be maintained in view of the disclaimer of *S. virginiae* added to claim 15 by the present amendment.

Inasmuch as neither Horinouchi, et al nor Kawachi, et al identically disclose or describe all of the claimed recitations of applicants' claims 15 and 19-23, the §102 rejections of claims 15 and 19-23 based on those two references are untenable and should be withdrawn.

In view of the present amendment and the foregoing remarks, it is respectfully requested that the objections and rejections set forth in the March 19, 2004 official action be withdrawn and that this application be passed to issue, and such action is earnestly solicited.

Respectfully submitted,

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A handwritten signature in dark ink, reading "Patrick J. Hagan", is written over a horizontal line.

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